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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,827	10/24/2005	Thomas Schwarz	BB-149	5864
23557 7590 03/03/2009 SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO Box 142950 GAINESVILLE, FL 32614				
EXAMINER				
HISSONG, BRUCE D				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/539,827

Applicant(s)

SCHWARZ ET AL.

Examiner

Bruce D. Hissong, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 October 2008.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 5-18 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1 and 5-18 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
3) ☐ Information Disclosure Statement(s) (PTO/CDC)
4) ☐ Interview Summary (PTO-413)
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____
Paper No(s)/Mail Date _____

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 6/11/2008, including arguments/remarks and amended claims, was received on 10/13/2008 and has been entered into the record.

2. In the response received on 10/13/2008, the Applicants cancelled claims 2-4. Therefore, claims 1 and 5-18 are pending and are the subject of this office action.

Claim Objections

The Examiner suggests the syntax of claim 1 can be improved by amending the claim to recite "a disorder of the skin associated with damage" rather than "a disorder of the skin, associated with damage".

Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 5-18 remain rejected under 35 USC § 112, first paragraph, regarding lack of enablement for methods of preventing or treating disorders of the skin associated with damage induced by UV-radiation, as set forth on pages 2-3 of the office action mailed on 6/11/2008.

In the response received on 10/13/2008, the Applicants argue that the scope of the invention has been narrowed by amending the claims to recite only treatment of sunburn, inflammation, and skin aging. The Applicants further argue that for an invention to be enabled, the specification need only to teach one of skill in the art "how to make" and "how to use" the invention, and that enablement is not precluded by the necessity for merely routine experimentation. The Applicants assert that the specification is enabling for the currently claimed invention because the specification provides guidance showing how to practice the claimed invention without undue experimentation, and also discloses multiple examples demonstrating the effectiveness of the claimed invention.

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These arguments have been fully considered and are not persuasive. The specification provides guidance and examples of *in vitro* experiments showing that pre-treatment with IL-18 decreased DNA damage induced by UV radiation, and 2 *in vivo* experiments showing that mice receiving IL-18 prior to UV irradiation exhibited less DNA damage and incidence of apoptotic "sunburn cells" compared to mice which did not receive IL-18. Although this data would show a person of ordinary skill in the art that the claimed method would treat sunburn and skin aging, it is noted that as written, the claims read broadly on treatment of any type of inflammation of the skin. It is well-known in the art that IL-18 acts as a pro-inflammatory cytokine, and Park *et al* (*Exp. Dermatol.*, 2006, Vol. 15, p. 589-595) demonstrated that administration of an agent, tannic acid, which *decreased* IL-18 production was beneficial for treating skin inflammation (see abstract; p. 591-593). Therefore, one of ordinary skill in the art would not necessarily predict that administration of IL-18, as currently claimed, would be effective in treating all types of skin inflammation, but instead would predict that IL-18 administration would exacerbate skin inflammation. Furthermore, Schwarz *et al* (*J. Immunol.*, 2006, Vol. 176, p. 2896-2901) teaches that although IL-18 decreases UV radiation DNA damage and thus may be an effective therapeutic agent for reducing UV radiation induced damage and treating skin cancer, "IL-18 is a proinflammatory cytokine, and thus topical application might induce inflammatory reactions" (paragraph bridging p. 2899-2900). Thus, one of ordinary skill in the art, guided by the examples of the specification and the teachings of the relevant art, would know that IL-18 administration would decrease DNA damage induced by UV radiation and be useful for treatment of disorders such as sunburn or skin aging, but would not predict that IL-18 administration would be therapeutically effective for treatment of all types of skin inflammation due to its ability to induce inflammation.

Therefore, due to the excessive breadth of the claims regarding prevention or treatment of all types of skin inflammation, the lack of guidance and examples showing that inflammation can be prevented or treated by the claimed method, and the unpredictability taught by the relevant art regarding the proinflammatory nature of IL-18, one of ordinary skill in the art would require further, undue experimentation in order to prevent or actually treat all types of skin inflammation by administration of IL-18.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection maintained:

1. Claims 1, 5-11, 13, and 15-16 remain rejected under 35 USC § 102(b) as being anticipated by Osaki *et al* ("Osaki" – J. Immunol., 1998, Vol. 160, p. 1742-1749), as set forth on pages 4-5 of the office action mailed on 6/11/2008. The claims of the instant invention are drawn to methods of preventing or treating a disorder of the skin associated with damage induced by UV radiation, wherein said method comprises administration of an effective amount of IL-18, wherein said disorder is sunburn, inflammation, or skin aging. The claims are further drawn to administration of various doses of IL-18 and via various routes of administration.

Osaki teaches administration of IL-18 to mice for treatment of melanoma (p. 1743, 1st column, 2nd paragraph). Osaki specifically teaches intraperitoneal administration of IL-18 at various doses, including 1 µg once a day (see p. 1743, 2nd column, 1st paragraph).

In the response received on 10/13/2008, the Applicants argue that Osaki does not anticipate the presently claimed invention because Osaki teaches treatment of melanoma, while the currently amended claims do not recite treatment of skin cancer.

These arguments have been fully considered and are not persuasive. It is known in the art that melanoma is associated with skin inflammation (see Coussens *et al*, *Nature*, 2002, Vol. 420, p. 860-867, specifically see Table 1). Therefore, by teaching a method of treating melanoma by administration of IL-18, Osaki necessarily teaches a method of treating a disorder associated with skin inflammation. For these reasons and those set forth on p. 4-5 of the previous office action, Osaki anticipates the limitations of the present claims. It is noted that Coussens is not being used as a grounds for rejection, but rather to show what was known in the art regarding melanoma and skin inflammation.

Rejection withdrawn:

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2. Rejection of claims 1, 5-13, and 15-18 under 35 USC § 102(e) as being anticipated by Gillespie *et al* ("Gillespie" – US 6,896,880), as set forth on page 5 of the office action mailed on 6/11/2008 is withdrawn.

In the response received on 10/13/2008, the Applicants argue that Gillespie focuses on treatment of diseases with excessive osteoclast formation, and therefore does not teach or suggest prevention or treatment of the presently claimed skin disorders selected from sunburn, inflammation, and skin aging.

This argument has been fully considered and is persuasive. Accordingly, this rejection is hereby withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection maintained:

1. Claim 14 remains rejected under 35 USC § 103(a) as being obvious in view of Osaki *et al*, as set forth on page 6 of the office action mailed on 6/11/2008. The subject matter of the presently claimed invention and the disclosure of Osaki are discussed *supra*. Claim 14 is further drawn to administration of IL-18 at a dose range from 0.1 µg/kg body weight to 100 µg/kg body weight.

In the response received on 10/13/2008, the Applicants argue that claim 14 is not obvious in view of Osaki because the method of Osaki is one of treating melanoma while the presently claimed invention does not recite treatment of skin cancer, and thus one of ordinary skill in the art would have no reason to modify the teachings of Osaki to arrive at the present invention.

These arguments have been fully considered and are not persuasive. Although Osaki does not specifically teach a method of treating sunburn or skin aging, it does teach a method of treating melanoma, which can be considered as a method of treating skin inflammation, as discussed above. Therefore a person of ordinary skill in the art would be motivated to optimize the administered dose of IL-18, and any dose optimization to within the currently claimed range would necessarily meet the limitations of the claims regarding treatment of skin inflammation.

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Rejection withdrawn:

2. Rejection of claim 14 under 35 USC § 103(a) as being obvious in view of Gillespie *et al.*, as set forth on page 6 of the office action mailed on 6/11/2008, is withdrawn.

In the response received on 10/13/2008, the Applicants argue that claim 14 is not obvious in view of Gillespie because the method of Gillespie is one of treating a patient with excessive osteoclast formation while the presently claimed invention does not recite treatment of skin cancer, and thus one of ordinary skill in the art would have no reason to modify the teachings of Gillespie to arrive at the present invention.

These arguments have been fully considered and are persuasive. Accordingly, the rejection is hereby withdrawn.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong

Art Unit 1646

/Gary B. Nickol /

Supervisory Patent Examiner, Art Unit 1646